

### **REMARKS**

Claims 1-18 and 28-29 have been examined and stand rejected under 35 U.S.C §§ 112, first paragraph (enablement), and/or 102. Claims 19 and 20 have been previously cancelled. Claims 21-27 have been withdrawn as directed to non-elected subject matter. Applicants have amended claims 1, 7 and 13 to delete the recitation of “or protein” and add the limitation contained in claims 2, 8 and 14. Claims 2, 3, 8, 9, 14, 15, 28 and 29 have been cancelled. No new matter has been added by these amendments.

#### **REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH, ENABLEMENT**

Claims 1, 4-13 and 16-18 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner contends that the specification does not enable one to identify the genotype of a person using a protein. Applicants have amended claims 1, 7 and 13 to delete the recitation of “protein” from the claims. Accordingly, withdrawal of this rejection is respectfully requested.

#### **REJECTION UNDER 35 U.S.C. § 102**

Claims 1, 4-13 and 16-18 have been rejected under 35 U.S.C. § 102(b) as anticipated by Väisänen.<sup>1</sup>

#### **I. THE RECITED INVENTION**

Claims 1, 7, and 13 are directed to methods of decreasing the level of t-PA antigen; preventing cardiovascular disease; or ameliorating cardiovascular disease respectively. The methods comprise detecting at least one 4G allele at the plasminogen activator inhibitor-1 (PAI-1) gene promoter site in the subject, and engaging the subject in exercise training for a period of time sufficient to decrease the level of t-PA antigen. These claims have been amended to recite “wherein the genotype is 4G/5G.” Claims 4-6 depend from claim 1. Claims 10-12 depend from claim 7. Claims 16-18 depend from claim 13.

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<sup>1</sup> Väisänen *et al.*, “Regular exercise, plasminogen activator inhibitor-1 (PAI-1) activity and 4G/5G promoter polymorphism in the PAI-1 gene,” THROMB. HAEMOST (1999) 82: 1117-1120.

In summary, the claims share the following common limitations – detecting a 4G/5G genotype at the PAI-1 gene and engaging the subject in exercise.

## II. THE CITED REFERENCES

Väisänen discloses identifying subjects having 4G/4G, 4G/5G, and 5G/5G genotypes.<sup>2</sup> Väisänen's research involved splitting one cohort into an exercise group and a reference group.<sup>3</sup> The study did not control for other genetic factors. For example, individuals within Väisänen's exercise group could have had other genetic factors not found in the reference group that distorted the results. Furthermore, Väisänen states that "regular exercise may be effective for controlling PAI-1 level in subjects *homozygous* for the 4G allele."<sup>4</sup> Furthermore, Väisänen's data shows that the 4G/5G individuals in the exercise group did not have a significant change in PAI-1 activity as compared to the 4G/5G individuals in the reference group.<sup>5</sup>

## III. ARGUMENT

For a reference to anticipate a claimed invention, the reference must teach each and every limitation recited in the claim. Väisänen does not teach that placing a person with a 4G/5G genotype on an exercise regime will benefit that person. Instead, it teaches that only homozygotes for the 4G allele will benefit. Therefore, Väisänen does not anticipate the recited invention, and reconsideration and withdrawal of this rejection are respectfully requested.

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<sup>2</sup> Väisänen at page 1118.

<sup>3</sup> Väisänen at page 1118

<sup>4</sup> Väisänen at page 1117 (emphasis added).


<sup>5</sup> Väisänen at page 1118

### CONCLUSION

In view of the foregoing amendments to the claims and remarks, Applicants respectfully submit that the specification and claims are in condition for allowance. Accordingly, reconsideration and withdrawal of the asserted objections and rejections, and allowance of pending claims 1, 4-13, and 16-18, are respectfully requested. Rejoinder of withdrawn claims 21-27 is also requested.

Respectfully submitted,

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